

Attorney Docket No.: 54704.8036.US03 (UMD-0072)
Inventors: John Langenfeld
Serial No.: 10/692,824
Filing Date: October 23, 2003
Page 17

REMARKS

Claims 1, 14, 16 and 18 are pending in the instant application. Claims 1, 14, 16 and 18 have been rejected. Claims 1 and 16 have been amended. No new matter has been added by these amendments to the claims. Reconsideration is respectfully requested in light of the claim amendments and the following remarks.

I. Priority

The Examiner has denied benefit of priority in the instant application to copending U.S. Application No. 10/044,716, filed January 11, 2002, which in turn claims benefit of U.S. Provisional Application No. 60/261,252, filed January 12, 2001. The Examiner suggests that the priority applications fail to provide an enabling disclosure for the invention of the instant application. Applicant disagrees with the Examiner's conclusions.

As acknowledged by the Examiner, the copending application discloses *in vivo* data showing that BMP-2 enhances formation of blood vessels around a tumor in a nude mouse. Further review of the application shows that it is BMP-2 that is indeed linked to the increased vascularization response *in vivo* in a well-established

Attorney Docket No.: 54704.8036.US03 (UMD-0072)
Inventors: John Langenfeld
Serial No.: 10/692,824
Filing Date: October 23, 2003
Page 18

animal model of tumor growth. It is a general principle of biology and pharmacology that if an agent has been shown to enhance a response, then inhibition of the agent's activity is a direct strategy for producing the opposite effect, in this case inhibition of vascularization. Therefore, one of skill would understand from the teachings of the priority application that BMP-2 regulates tumor vascularization and that vascularization could be inhibited by inhibiting activity of BMP-2. Therefore, the copending application and its provisional parent contain disclosure that would enable one of skill to develop the methods of the instant invention. Applicant respectfully requests reconsideration of the claim for priority.

II. Specification

The specification has been objected to because of numerous improperly demarcated trademarks. Applicant has amended the specification to correct this issue. The specification has also been objected to because of a misspelling of "ABI Prism" Applicant has corrected the typographical error. Finally, the disclosure has been objected to because it refers to embedded hyperlinks, which is not permissible. Applicant has removed such references from the

Attorney Docket No.: 54704.8036.US03 (UMD-0072)
Inventors: John Langenfeld
Serial No.: 10/692,824
Filing Date: October 23, 2003
Page 19

disclosure. Accordingly, withdrawal of these objections is respectfully requested.

III. Rejection of Claims Under 35 U.S.C. 112, First Paragraph

Claims 1, 14, 16 and 18 have been rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement because the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Examiner suggests that the claims recite administering a therapeutically effective amount of a "BMP-2 activity inhibitor" whereas the specification fails to provide adequate description of all such possible substances. Applicant respectfully traverses this rejection.

Applicants have amended claims 1, 14, 16 and 18 to recite that the BMP-2 activity inhibitor of the claims is one specific BMP-2 activity inhibitor. Support for this amendment to the claims can be found throughout the specification as filed but in particular at pages 6-7 and pages 24-25 where the specific BMP-2 activity inhibitors are disclosed. As acknowledged by the Examiner, the specification as filed contains specific description of certain

Attorney Docket No.: 54704.8036.US03 (UMD-0072)
Inventors: John Langenfeld
Serial No.: 10/692,824
Filing Date: October 23, 2003
Page 20

BMP-2 activity inhibitors, including the one now listed in the claims as amended. Therefore, the claims as amended meet the requirements of 35 U.S.C. 112, first paragraph. Withdrawal of this rejection is respectfully requested.

Claims 1, 14, 16 and 18 have been rejected under 35 U.S.C. 112, first paragraph as failing to comply with the enablement requirement because the claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the relevant art to make and use the invention without undue experimentation. The Examiner suggests that there is not a reasonable correlation between the scope of the claims and the scope of enablement and that the claims to use of BMP-2 activity inhibitors lacks sufficient enablement. Applicant respectfully traverses this rejection.

At the outset, as discussed *supra*, Applicant has amended the claims to recite that the instant invention is a method that involves administration of a specific BMP-2 activity inhibitor. Support for this amendment to the claims can be found throughout the specification as filed and is the compound acknowledged by the Examiner to be specifically taught. Further, the claims have been amended to recite that the tumor being treated is a tumor that overexpresses BMP-2. Support for this amendment can be found

Attorney Docket No.: 54704.8036.US03 (UMD-0072)
Inventors: John Langenfeld
Serial No.: 10/692,824
Filing Date: October 23, 2003
Page 21

throughout the specification as filed but in particular at pages 58-85 where the issue of overexpression of BMP-2 in tumors is taught and discussed.

Claims 1, 14, 16 and 18 are drawn not to a method of treating cancer or even inhibiting tumor growth but to a very specific effect, reducing vascularization of a tumor. In the specification as filed at page 58, experiments are described in mice where noggin is used and tumor vascularization is assessed. Then in figure 10 of the specification as filed, the results of the experiments are shown where there is a photograph of a tumor from a mouse treated with noggin, showing a lack of tumor vascularization as compared to the photographs of the mice not treated with noggin. Therefore, the specification as filed clearly provides *in vivo* evidence of the method of the instant invention where noggin, a BMP-2 activity inhibitor, was capable of reducing tumor vascularization *in vivo*. Therefore, contrary to the Examiner's suggestion, one of skill would understand how to make and use the method of the instant invention based upon the *in vivo* data as a method of reducing tumor vascularization. The nude mouse model used and described in the specification as filed is a well-accepted model for testing of potential therapeutic compounds for *in vivo* activity.

Attorney Docket No.: 54704.8036.US03 (UMD-0072)
Inventors: John Langenfeld
Serial No.: 10/692,824
Filing Date: October 23, 2003
Page 22

The specification also provides one of skill with additional details on the method of the present invention and the basis for understanding that BMP-2 activity inhibitors are likely candidates for inhibiting tumor growth in tumors that overexpress BMP-2. To make it clear that the tumor types being targeted are ones that overexpress BMP-2, the claims have been amended. At pages 58-85 of the specification as filed there is detailed discussion of the fact that tumors overexpress BMP-2 and that inhibiting activity of BMP-2 can result in inhibition of tumor growth through reduction in tumor vascularization. The literature described by the Examiner teaching a potential role for BMP-2 as a cancer treatment are not applicable as one of skill would, by reviewing the information in the specification as filed, understand that BMP-2 inhibition is desirable and that the results of others may involve other members of the bone morphogenetic protein family such as BMP-4, or involve tumor types that are not associated with overexpression of BMP-2. Additionally, the results of others referred to by the Examiner (Tada et al. 1998; Buckley et al. 2004; Hardwick et al. 2004; Haramis et al. 2004; Ghosh-Choudhury et al. 2000; Nakamura et al. 2003; Wen et al. 2004) rely on *in vitro* data. It is often the case that *in vitro* results will not always predict *in vivo* results. Therefore, with the results of the specification in hand, one of

Attorney Docket No.: 54704.8036.US03 (UMD-0072)
Inventors: John Langenfeld
Serial No.: 10/692,824
Filing Date: October 23, 2003
Page 23

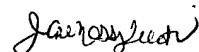
skill would understand that *in vivo* the effect of a BMP-2 inhibitor is to reduce tumor vascularization in tumors that overexpress BMP-2.

Accordingly, the claims as amended meet the requirements of 35 U.S.C. 112, first paragraph and withdrawal of this rejection is respectfully requested.

IV. Conclusion

Applicant believes that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,



Jane Massey Licata
Registration No. 32,257

Date: September 1, 2005

Licata & Tyrrell P.C.
66 E. Main Street
Marlton, NJ 08053

856-810-1515